

## REMARKS

In view of the foregoing amendments and the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

Claims 47-51 are pending in the present application. Claims 1-46 have been canceled without prejudice.

On page 3 of the Office Action, the Examiner rejected claims 35, 37, 39, 40, 42, 44 and 47-51 under 35 U.S.C. § 103(a) as being unpatentable over the teachings of Cutie et al., WO 01/82875 ("Cutie") in view of Lewis, WO 01/35940 ("Lewis") and further in view of Vergez et al., United States Published Patent Application No. 2006/0204578 ("Vergez").

Although Applicants do not agree with this rejection, in an effort to expedite prosecution of the present application, Applicants have canceled claims 1-46 without prejudice and respectfully request reconsideration of the rejection of claims 47-51.

Claims 47-51 recite a once a day metformin/pioglitazone tablet that consists of three essential elements: 1) a controlled release metformin core that is surrounded by a water insoluble semi-permeable membrane; 2) a primary seal coat applied to the semi-permeable membrane; and 3) an immediate release pioglitazone coating applied to the primary seal coat.

As explained in the prior submissions, Applicants discovered that a primary seal coat applied to the outer surface of the semi-permeable membrane of the metformin core improved the adhesion, release and stability of the immediate release pioglitazone layer. Applicants respectfully submit that the presently claimed structure is not rendered

obvious by the cited prior art because there is no suggestion to apply a seal coat to a semi-permeable membrane and then apply the immediate release pioglitazone to the seal coat.

In the Office Action, the Examiner identifies portions of each of the three references where individual elements of the pending claims can be found and then extracts these individual elements to arrive at the pending claims. Applicants respectfully submit that the Examiner is improperly employing hindsight to select individual elements from the references and combine the selected elements to arrive at the presently claimed invention without any motivation or guidance for the proposed selection or combination. For example, both Cutie and Vergez disclose dosage forms with two different drugs wherein both drugs are enclosed in a controlled release coating. The teachings of neither Cutie nor Vergez would lead a skilled artisan to a dosage form with one drug (metformin) released from a controlled release core and a separate and distinct drug (pioglitazone) released in an immediate release manner from a coating surrounding the controlled release core.

Moreover, neither Cutie nor Vergez would suggest to a skilled artisan placing a seal coating between the semipermeable membrane of a controlled release metformin core and an immediate release pioglitazone coating to overcome the adhesion, release and stability problems associated with the application of a pioglitazone coating to a semipermeable coating. The addition of Lewis would not overcome the deficiencies of Cutie and/or Vergez because Lewis does not relate to once a day dosage forms. Rather, Lewis describes only immediate release dosage forms and does not remotely suggest any manner for successfully applying an immediate release pioglitazone coating to a semipermeable membrane of a controlled release metformin core as recited in the

currently pending claims.

In the Office Action, the Examiner also indicated that Applicants prior arguments had been considered but were not deemed persuasive, in part, because the Examiner believed Applicants were attempting to “show nonobviousness by attacking the references individually”. September 29, 2009 Office Action, p. 11. Applicants respectfully dispute this contention. In the prior submission, Applicants did not attack the cited references individually. Rather, Applicants explained what each individual reference taught and then explained what they believed a combination of the references (as suggested by the Examiner) would suggest to a skilled artisan. It is undisputed that the references individually do not render the present claims obvious. Applicants respectfully repeat the arguments that the proposed combination also would not render the present claims obvious.

Specifically, Cutie discloses a core formulation comprising a first layer comprising pioglitazone which covers at least a portion of a core comprising the biguanide, metformin (i.e. glucophage). The core formulation of Cutie which comprises both metformin and pioglitazone “may be coated with sugar, shellac or other enteric coating agents” (p. 7, lines 9-11” and “can have an outer shell made of biodegradable material (including cellulosic polymers, polyvinyl acetate and polyvinyl alcohol).” Cutie, p. 7, lines 13-28. The “core formulation” of Cutie contains both metformin and pioglitazone and not a core containing only metformin.

Vergez teaches a “dual controlled release dosage form” wherein the dosage form contains at least two active ingredients that are released from the dosage form in a

controlled release manner. *See generally*: Vergez ¶¶ 2, 15 and 22. Vergez describes a number of ways in which the dual controlled release dosage is prepared but never discloses or suggest a dosage form wherein the metformin is surrounded by a semi-permeable membrane, and then an immediate release pioglitazone is applied to a seal coated semipermeable membrane surrounding the controlled release metformin core.

Lewis teaches an immediate release dosage form containing immediate release forms of both metformin and pioglitazone. There is no mention, disclosure or suggestion in Lewis of preparing a controlled release metformin core and an immediate release pioglitazone layer as required by the pending claims. At best, Lewis teaches that the metformin and pioglitazone components should be separated by an inert barrier. This teaching of Lewis, when added to Cutie and/or Vergez, merely suggests to the skilled artisan that the metformin and pioglitazone components in a controlled release core should be separated by an inert layer. The teaching of Lewis does not motivate or lead a skilled artisan to modify the teachings of Cutie and/or Vergez to remove the pioglitazone component from the controlled release core and apply a seal coating to the semipermeable membrane of the controlled release core prior to the application of an immediate release pioglitazone coating as required by the pending claims.

Applicants respectfully submit the combination of Cutie, Lewis and Vergez would not lead a skilled artisan to the presently claimed invention. Rather, the combination of Cutie, Lewis and Vergez would lead a skilled artisan to prepare a dosage form consisting of a controlled release core comprising both metformin and pioglitazone components wherein the metformin and pioglitazone in the controlled release core are separated by an

inert barrier layer.

On page 12 of the Office Action, the Examiner maintained the provisional non-statutory obviousness-type double patenting rejection of the claims based upon co-pending Application No. 11/094,493. As indicated in the prior submission, Applicants respectfully request this rejection be held in abeyance pending the finding of allowable subject matter in either the present application or Application No. 11/094,493.

If the Examiner believes the currently pending claims are allowable, Applicants respectfully submit that the provisional double patenting rejection should be withdrawn and a Notice of Allowance issued in accordance with MPEP § 804(I)(B)(1). MPEP § 804(I)(B)(1) reads in relevant part as follows:

If a “provisional” nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier filed application to issue as a patent without a terminal disclaimer.

The present application was filed on September 19, 2003, and Application No. 11/094,493 was filed on March 30, 2005. Based upon these filing dates and the current status of both applications, Applicants submit that MPEP § 804(I)(B)(1) is applicable to the present provisional nonstatutory obviousness-type double patenting rejection. Upon a finding of allowable subject matter in the present application, MPEP 804(I)(B)(1) requires the withdrawal of the provisional double patenting rejection and the issuance of a Notice of Allowance.

Based upon the foregoing amendments and representations, Applicants respectfully request that the rejection of the claims in the above-identified application be withdrawn. Early and favorable action is earnestly solicited.

Respectfully submitted,

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